Section 1 Introduction

Chapter 1

History of perioperative hypothermia

Perioperative hypothermia is one of the oldest known side effects of general anaesthesia and is still a very common problem today.

First description of perioperative hypothermia

Perioperative hypothermia was first described by Ernst von Bibra and Emil Harlass in Erlangen (Germany) in the book *Die Wirkung des Schwefeläthers in chemischer und physiologischer Beziehung* (Fig. 1.1) in the year 1847, only 1 year after the first successful general anaesthesia was performed by Thomas Green Morton in Boston.

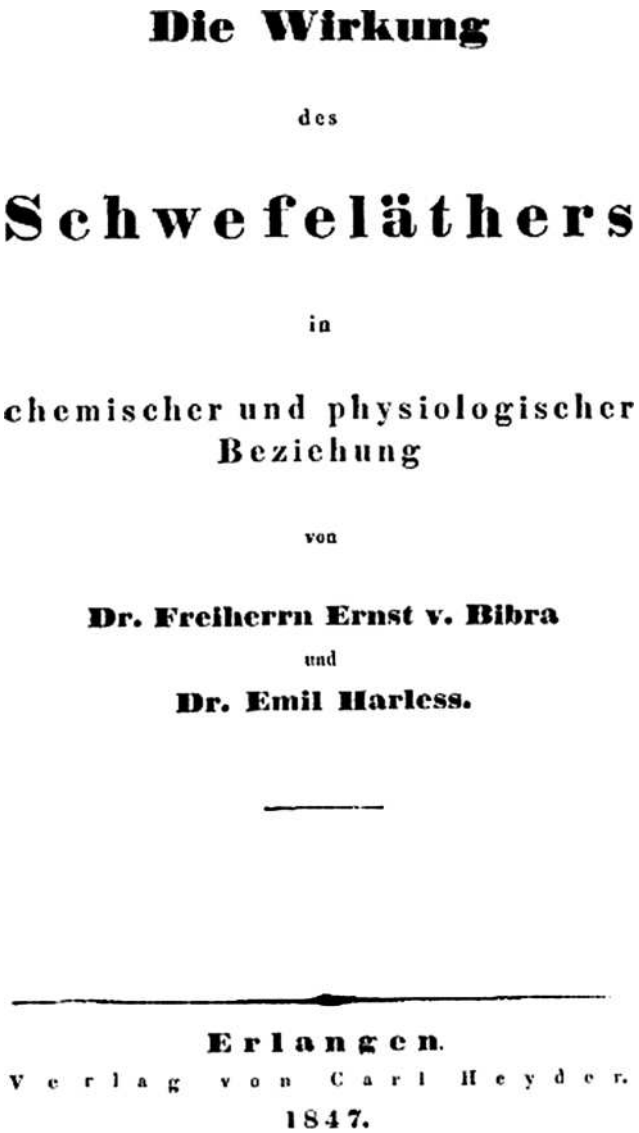
In this book von Bibra and Harness describe results from human and animal experiments with sulfuric ether. The authors describe that the pharyngeal temperature of a rabbit had fallen to 24.5 °Réaumur under ether anaesthesia, which corresponds to a temperature of 30.6 °C. In contrast, a normal heathy rabbit had a pharyngeal temperature of 31.5 °Réaumur (= 39.4 °C). However, these results of a drop in core temperature under anaesthesia did not get very much attention as there were many more important problems associated with anaesthesia at that time.

Measurement of core temperature and definition of hypothermia

In the middle of the nineteenth century Carl Reinhold August Wunderlich introduced thermometry and temperature charts into hospitals and declared thermometry imperative in ill patients.

In 1868 Wunderlich published the book *Das Verhalten der Eigenwärme in Krankheiten*, in which he analysed over 1 million axillary temperature recordings from some 25 000 patients. He identified 37.0 °C as the mean temperature of healthy adults and declared that the normal temperature range extends from 36.25 °C to 37.5 °C.

A core temperature below 36 °C was only found in very severe illness. In his opinion a core temperature below 36.25 °C should only be considered to be normal under special circumstances. This may be the first scientific definition of hypothermia.


Die Wirkung

des

Schwefeläthers

in

chemischer und physiologischer Beziehung

von

Dr. Freiherrn Ernst v. Bibra

und

Dr. Emil Harless.

Erlangen.

Verlag von Carl Heyder.

1847.

Fig. 1.1 Cover of the book *Die Wirkung des Schwefeläthers in chemischer und physiologischer Beziehung* by von Bibra and Harness. (Reproduced from: Von Hintzenstern U, Petermann H and Schwarz W. Frühe Erlanger Beiträge zur Theorie und Praxis der Äther- und Chloroformnarkose. Teil 2. Die tierexperimentellen Untersuchungen von Ernst von Bibra und Emil Harless. Anaesthesist 2001; **50**: 869–880 [1] with kind permission of Springer Science and Business Media.)

First descriptions of adverse effects of perioperative hypothermia and first measures against hypothermia

In 1880, von Kappeler described a decrease in body temperature in 20 surgical patients. In 1881, the gynaecologist Emil Schwarz from Halle in Germany recommended warming infusion fluids to 38–40 °C to prevent cooling of the body. In 1907 Döderlein and König described an association between postoperative pneumonia and perioperative hypothermia. They recommended warmed operating tables, which could reduce pneumonia rates that ranged between 7.5 to 10.2% down to 3.6 to 2.1%. In the same year the surgeon Christian Heinrich Braun from Göttingen in Germany tried to prevent hypothermia

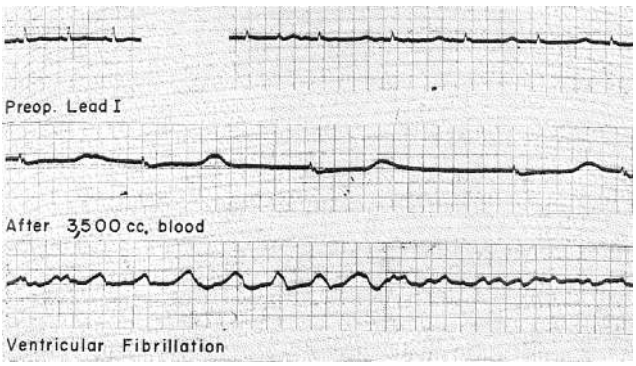


Fig. 1.2 Original electrocardiogram (ECG) recording in a patient with massive transfusion of cold blood. (Reproduced from: Howland WS, Boyan CP, Schweizer O. Ventricular fibrillation during massive blood replacement. Am J Surg 1956; **92**: 356–360 [2] with permission of Elsevier.)

during surgery by placing the patients on warm water cushions and by covering them with warm towels.

Severe perioperative hypothermia as a cause of death during massive transfusions

In 1956, Howland *et al.* [2] described nine cases of ventricular fibrillation during abdominal operations that were associated with rapid massive transfusion of cold blood. They speculated that one of the important pathophysiological factors was that cold blood was delivered directly to the heart, thereby causing cooling of the myocardium and leading to cardiac arrhythmias and ventricular fibrillation (Fig. 1.2).

In a subsequent prospective study [3] an oesophageal temperature probe was used to measure core temperature as close to the heart as possible during a massive transfusion of blood. In the first patient, the core temperature only dropped from 37 °C to 36 °C during the first 3000 ml of blood transfusion. During the following 120 minutes the patient needed 18 000 ml of cold bank blood at an average rate of 150 ml min^{-1}. During this period the oesophageal temperature decreased steadily. At 31 °C the first ventricular extrasystoles appeared and at 29 °C there was a marked prolongation of the ST-interval followed by bradycardia and ventricular extrasystoles. All cardiac function ceased at 27.5 °C although the estimated blood loss had been completely replaced.

In another patient, asystole appeared at a core temperature of 32 °C after transfusion of 6 600 ml of cold blood. Several other patients developed severe hypothermia during massive transfusions with core temperatures of about 30 to 32 °C. Because of these observations the authors decided to transfuse warm blood after the third unit of banked blood had been administered. Therefore they used a blood warmer consisting of more than 7 meters of sterile plastic tubing placed in a 20 l water bath with a bath thermometer (Fig. 1.3). The temperature of this water bath was regulated by adding warm or cold water.

With this blood warmer subsequent patients remained relatively warm, well above 35 °C, during massive transfusions and none of them developed arrhythmia or cardiac arrest.

A few years later Churchill-Davidson stated that hypothermia was the most important problem in massive blood transfusions. Even if the blood has been partially warmed, a massive transfusion can reduce the body temperature to a dangerously low level [4].

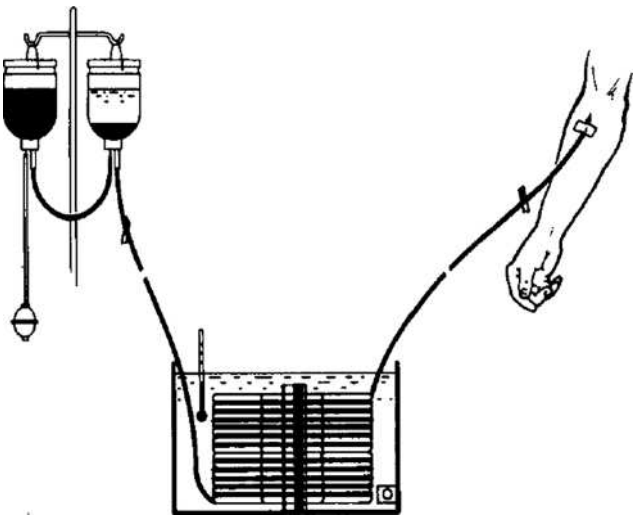


Fig. 1.3 Schematic drawing of the blood warmer. (Reproduced from: Boyan CP and Howland WS. Blood temperature: A critical factor in massive transfusion. Anesthesiology 1961; **22**: 559–563 [3] with kind permission of Wolters Kluwer Health.)

Severe perioperative hypothermia in paediatric anaesthesia

Another field where perioperative hypothermia was associated with severe problems was the emerging field of paediatric surgery and anaesthesia. In 1957, France [5] described relevant drops in core temperature down to 28.6 °C in newborns. The hypothermic children were drowsy with a slow respiration and rewarming took several hours. Hacket and Crosby [6] found that postoperative feeding problems in infants were associated with a fall in the core temperature below 36.1 °C. In 1962, Farman described an association of severe perioperative hypothermia with perioperative death in babies [7]. Nine of 67 babies undergoing surgery died within the first 24 hours; six of them suffered from hypothermia, with temperatures below 36.1 °C.

The major cause of death in the hypothermic babies was respiratory depression [7].

In this article, Farman also searched for risk factors for perioperative hypothermia. He discussed an association with:

- Severity of illness
- Effect of low body weight
- Young age
- Anaesthetic drugs
- Muscle relaxants
- Long operations
- Air conditioning.

Harrison *et al.* [8] added:

- Intra-abdominal or intrathoracic procedures
- Low initial core temperature
- Transfusion of cold blood.

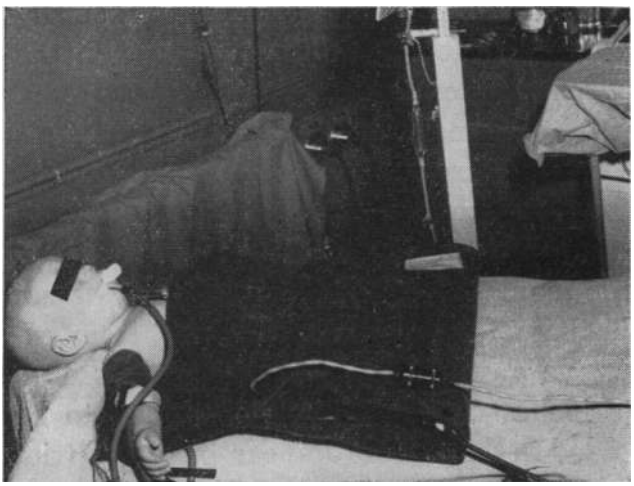


Fig. 1.4 Electrical heating blanket to maintain normothermia for a craniotomy in an infant. (Reproduced from: Bering EA Jr, Matson DD. A technique for the prevention of severe hypothermia during surgery of infants. Ann Surg 1953; **137**: 407–409 [11] with kind permission of Wolters Kluwer Health.)

First warming devices against perioperative hypothermia

Severe hypothermia in children and the dramatic observations of deaths due to perioperative hypothermia led to the development of several warming devices. In addition to blood and fluid warming devices [9, 10] heating mattresses were developed. In 1953, Bering and Matson [11] successfully used an electrical heating blanket to maintain normothermia during neurosurgical operations in infants (Fig. 1.4). The blanket measured about 60 × 100 cm overall, but was designed to be folded in the middle and closed with snap buttons on two sides. This allowed its use as a bottom or top blanket or to cover the patient on all sides. The temperature of this electrical heating mattress was controlled by a ten-step regulator switch and had a maximum temperature of slightly over 43 °C. The authors were convinced that the early postoperative recovery of infants undergoing all types of major neurosurgical procedure was strikingly accelerated when severe hypothermia had been obviated (Fig. 1.5).

In 1962, Calvert [12] described the use of a circulating water mattress in babies (Fig. 1.6). This rubber mattress was placed on the operating table and warm water from the hot and cold supply of the theatre continually circulated through the mattress. The temperature was regulated by varying the proportions of hot and cold water flowing through the mattress using a thermostatic mixing valve (Fig. 1.7).

They observed that the infants in their control group had a difference between preoperative and postoperative core temperature of 2.4 °C, whereas the infants that were warmed with the water mattress had an overall drop in core temperature of only 0.3 °C.

In 1973, Lewis *et al.* [13] described the first forced-air warming system for infants and could prove the efficacy of the system (Figs. 1.8 and 1.9).

With all these measures it was possible to prevent severe hypothermia. However, in the early 1980s as many as 50 to 80% of all patients still arrived hypothermic in the recovery room [14]. At that time mild perioperative hypothermia was considered a normal consequence of surgery, and not thought to be especially harmful. The only serious complication was thought to be the common postoperative shivering, because it

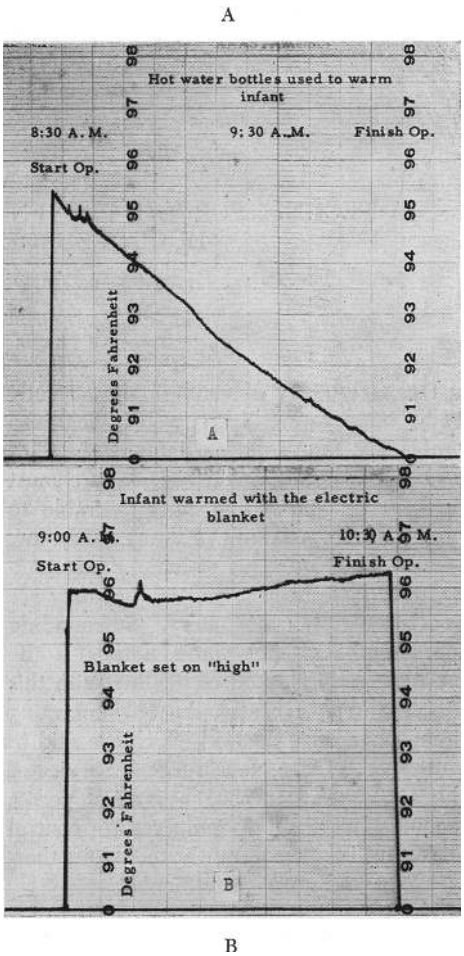


Fig. 1.5 Original recording of the rectal temperature of two infants during hydrocephalus operations. The first infant was warmed with hot water bottles as usual and the operation ended with a core temperature of 90 °F = 32.2 °C, whereas the second infant was warmed with the electrical heating blanket and the operation ended at a core temperature of 96.4 °F = 35.8 °C. (Reproduced from: Bering EA Jr, Matson DD. A technic for the prevention of severe hypothermia during surgery of infants. Ann Surg 1953; **137**: 407–409 [11] with kind permission of Wolters Kluwer Health.)

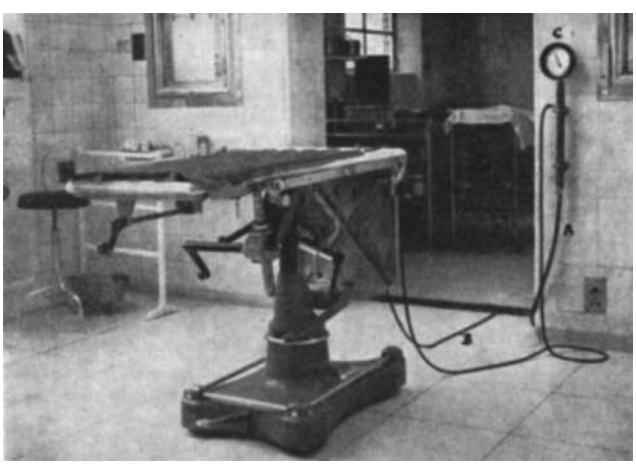


Fig. 1.6 The hot water mattress in position on the table. (Reproduced from: Calvert DG. Inadvertent hypothermia in paediatric surgery and a method for its prevention. Anaesthesia 1962; **17**: 29–45 [12] (Copyright by John Wiley and Sons) with kind permission of John Wiley and Sons.)

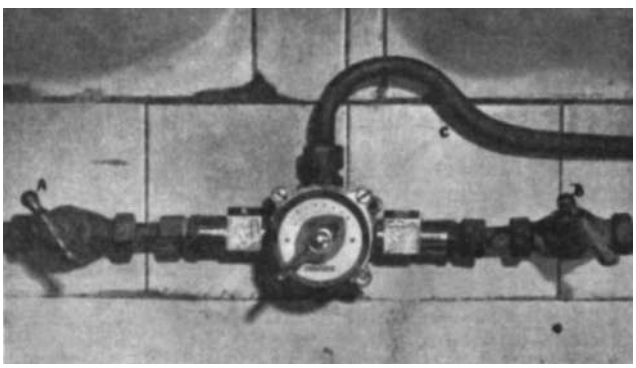


Fig. 1.7 The mixing valve controlling the water temperature in the mattress. (Reproduced from: Calvert DG. Inadvertent hypothermia in paediatric surgery and a method for its prevention. Anaesthesia 1962; **17**: 29–45 [12] (Copyright by John Wiley and Sons) with kind permission of John Wiley and Sons.)

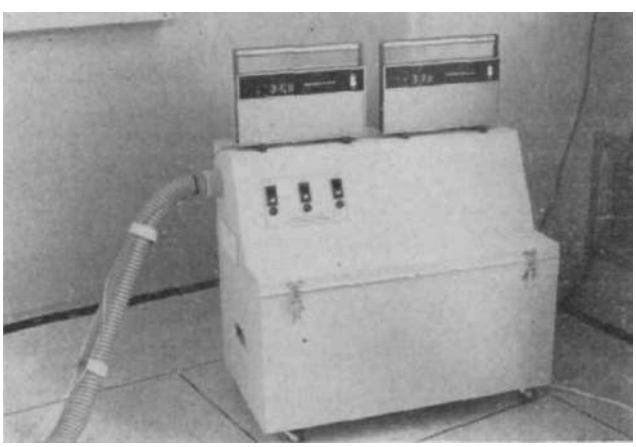


Fig. 1.8 The controller of the forced-air warmer used by Lewis. (Reproduced from: Lewis RB, Shaw A, Etchells AH. Contact mattress to prevent heat loss in neonatal and paediatric surgery. Br J Anaesth 1973; **45**: 919–922 [13] with kind permission of Oxford University Press.)

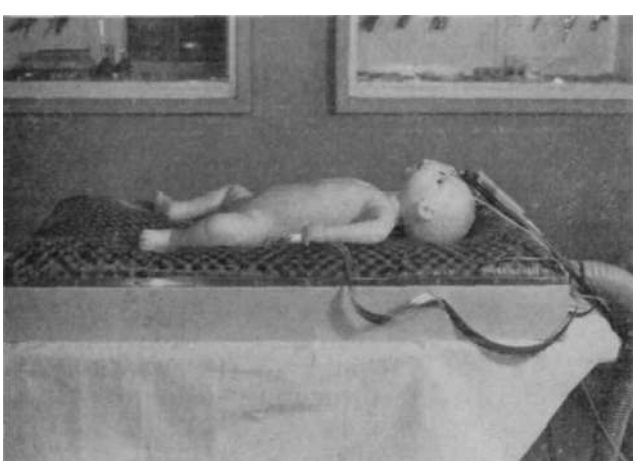


Fig. 1.9 The underbody forced-air warmer blanket used by Lewis. (Reproduced from: Lewis RB, Shaw A, Etchells AH. Contact mattress to prevent heat loss in neonatal and paediatric surgery. Br J Anaesth 1973; **45**: 919–922 [13] with kind permission of Oxford University Press.)

can increase oxygen demand and oxygen uptake [15]. Perioperative hypothermia was assumed to be caused by anaesthetics that switch off all thermoregulatory defences and by excessive heat loss to the environment [16].

In the next 20 years, new concepts for intraoperative thermoregulation were described and the adverse side effects of mild perioperative hypothermia were discovered [16]. Additionally:

- Postoperative rewarming strategies were developed
- Drugs against postoperative shivering were extensively tested
- Intraoperative warming devices were developed and evaluated
- Prewarming was described and evaluated.

Altogether this led to the publication of several national guidelines, e.g.:

- The National Institute for Health and Care Excellence (NICE) guideline [17]
- The American Society of Perianesthesia Nurses (ASPAN) guideline [18]
- The evidence-based guideline for prevention of perioperative hypothermia of the Canadian Association of General Surgeons [19]
- The German and Austrian guideline [20].

Section 1 Introduction

Chapter 2

Physiology of heat and cold sensation

To understand the core and peripheral temperature changes occurring during anaesthesia and surgery, a basic knowledge of the physiology of heat and cold sensation, thermoregulation and heat exchange of the body is necessary. In this chapter, a brief and simplified overview of the physiology of heat and cold sensation is given. The following two chapters will give overviews of thermoregulation and heat exchange between the body and the environment.

The physiology of heat and cold sensation, thermoregulation and heat exchange of the body are very complex. For the anaesthesia provider, not every detail is of clinical importance. A basic knowledge of the processes is sufficient.

Thermosensation is one the most ancient sensory processes and is present in all organisms [21]. In humans, the thermal information is generated by special thermoreceptors and transported to the brain using specialised nerve fibres and pathways.

Heat and cold sensation has at least four physiological functions:

1. The afferent heat and cold signals help to identify objects and materials through touch [22]. For example, metals can be easily discriminated from plastic with the help of the thermal information because metals have a high heat capacity and therefore stay cold longer in the hand compared to plastic.
2. The afferent heat and cold signals help to perceive a 'feeling' from the body if it is warm or cold. This is part of the general sense of the physiological condition of the body, also called interoception [23].
3. The afferent heat and cold signals help to detect potentially noxious thermal stimuli that pose a threat to the integrity of the skin (e.g. burns). Information about noxious temperature is detected and transported by different special thermoreceptors and nerve fibres from information about innocuous temperature.
4. The afferent heat and cold signals are signals for autonomic thermoregulation. The core body temperature of humans is tightly regulated under normal circumstances. To allow thermal regulation, adequate temperature sensing of the core of the body and the body surface is necessary.

Thermoregulation is only one function of the sensation of heat and cold.

The following structures are involved in the process of heat and cold sensation:

1. Thermoreceptors
2. Thermosensitive neurons and their afferent nerve fibres
3. Neuronal pathways in the spinal cord and the brain
4. Special nuclei in the thalamus and hypothalamus
5. Cortex of the brain.

Thermoreceptors

Temperature is sensed in the free nerve endings of thermosensitive neurons by specific receptor proteins of the transient receptor potential (TRP) family of ion channels.

The TRP channels consist of six transmembrane protein domains. The functional channel is relatively non-selectively permeable to cations, including sodium, calcium and magnesium. The structure of one receptor protein (TRPV1) is shown in Fig. 2.1.

The basis of thermosensation lies in the property of these channels to conduct ions in a highly temperature-dependent manner.

In general, every biochemical reaction, every enzyme and ion channel, is to some degree temperature dependent. However, the steepness of this temperature dependence is different in distinct enzymes and ion channels and can be expressed and quantified using the dimensionless Q_{10} value. Q_{10} is defined as the relative change in reaction rate upon a 10 °C increase in temperature. Ion channels typically have a Q_{10} value between

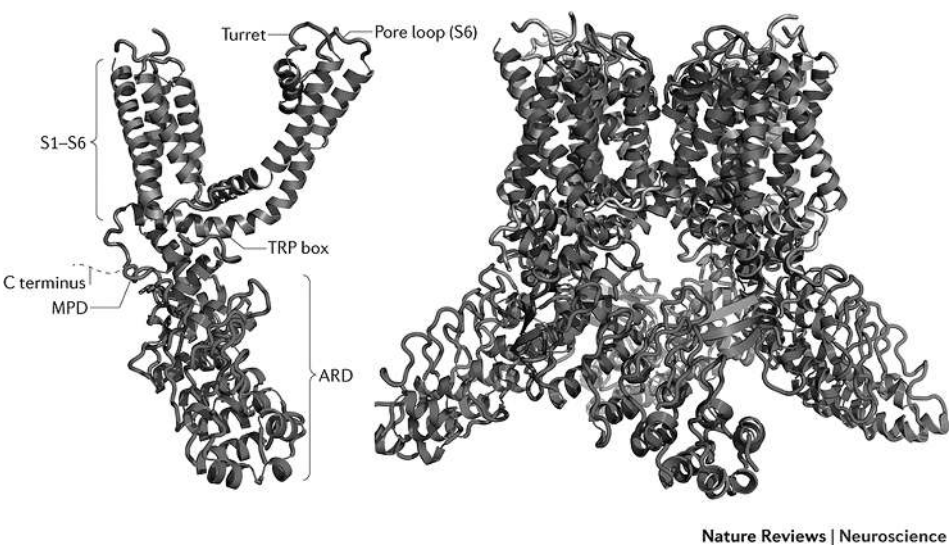


Fig. 2.1 The structure of a transient receptor potential (TRP) V1. (Reprinted by permission from Macmillan Publishers Ltd: Vriens J, Nilius B, Voets T. Peripheral thermosensation in mammals. Nat Rev Neurosci 2014; **15**: 573–589 [21].)